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The Effect of Maintenance Dose Vecuronium on Pre-established Metocurine- or Vecuronium-induced Neuromuscular Blockade

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When a long-acting muscle relaxant is administered at the start of an anesthetic, inadequate relaxation for some crucial period occasionally occurs near the end of the surgical procedure. One example might be the necessity for profound paralysis during peritoneal closure. A supplemental dose of the original muscle relaxant given at this time may be ineffective if the dose is small; a larger dose may prevent adequate reversal at the end of surgery. Aps and Inglis[1] have suggested that small doses of the intermediate duration muscle relaxants (atracurium and vecuronium) can be used to enhance and somewhat prolong the duration of neuromuscular blockade in the presence of residual pancuronium activity without adversely affecting the ability to antagonize the neuromuscular blockade at the end of surgery. To quantitatively evaluate the synergistic potential of this therapeutic regimen, this study was designed to compare the effect of a maintenance dose of vecuronium given during recovery from an initial dose of either metocurine or vecuronium.

MATERIALS AND METHODS

A total of 24 neurosurgical patients were studied with informed consent after approval from the Institutional Review Board. Patients with significant cardiovascular, renal, hepatic, or neuromuscular disease, as well as those receiving medications known to affect neuromuscular blockade, were excluded from the study. Based on the anticipated duration of the surgical procedure, patients were assigned to receive either metocurine 0.3 mg/kg or vecuronium 0.1 mg/kg during anesthetic induction. Preoperative medication was left to the discretion of the anesthesiologist assigned to each patient. Anesthesia was induced with thiopental 4–8 mg/kg iv and isoflurane 2% inspired in oxygen. The ulnar nerve was stimulated at the wrist with 0.2 ms duration supramaximal square-waves at 0.1 Hz from a Grass S-44 stimulator in conjunction with a SIU-4678 stimulus isolation unit. When the baseline neuromuscular response of the thumb adductors, as measured by an FT-10 force-displacement transducer, became stable, the bolus of the selected muscle relaxant was administered iv. After intubation the isoflurane concentration was reduced to 0.75% inspired in N_2O 66% and O_2. When the monitored twitch response recovered to 25% of baseline control, a maintenance dose of vecuronium 0.015 mg/kg was given. The maximum response after this second dose of relaxant and the times required for 5% and 25% recovery of baseline twitch height were recorded. In the event that the second dose of relaxant did not provide 95% paralysis, the time required for the commencement of recovery from the second dose was used instead of the 5% recovery time. Temperature was maintained above 35° C with the aid of heating blankets. End-tidal P_{CO_2} was maintained between 24 and 30 mmHg. Comparisons between groups were made with Student's two tailed t test for unpaired data. The threshold for significance was $P \leq 0.05$. Results are expressed as mean ± SD.

RESULTS

The results of this study are summarized in the table 1. There were no significant differences between groups in age or weight. The neuromuscular blocking response to maintenance doses of vecuronium was markedly enhanced in both magnitude and duration in patients initially receiving metocurine compared to those initially blocked with vecuronium. Although all patients initially receiving metocurine subsequently experienced complete neuromuscular blockade from the maintenance dose of vecuronium, four of the 12 patients initially given vecuronium did not attain 95% blockade with the maintenance dose.

DISCUSSION

Rashkovsky *et al.*[2] have shown that if at the time of 25% recovery from complete vecuronium or pancuronium neuromuscular blockade, 95% paralysis is reestablished with incremental doses of vecuronium, the required

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vecuronium dose and the duration of paralysis is dependent on the relaxant that was initially used. Patients initially paralyzed with pancuronium required approximately 25% less vecuronium and the time to recovery was twice that seen in patients initially paralyzed with vecuronium. This interaction between vecuronium and pancuronium was considered due to the different plasma clearances for these drugs and to the relative concentrations of these drugs at the receptor site, with the majority of receptors still occupied by pancuronium. Because combinations of vecuronium and pancuronium are simply additive in action,[3] synergism was not considered operative in that study.

The neuromuscular blockers chosen for the current study were selected on the basis of their lack of cardiovascular side effects. In light of previously acknowledged synergism with the combination of vecuronium and *d*-tubocurarine during anesthesia induction,[4] one might expect combinations of vecuronium and metocurine to be superadditive. The present study demonstrates similar synergism at the end of the surgical procedure, whereby the use of a small dose of vecuronium 0.015 mg/kg during the recovery phase from a preexisting metocurine blockade led to profound blockade of prolonged duration. Although the unblinded and nonrandom assignment of patients into the vecuronium and pancuronium groups may introduce some bias into this study, the results are nevertheless striking. The same vecuronium dose administered at 25% recovery from preexisting vecuronium blockade provides additional surgical relaxation (defined as the time to 25% recovery) lasting 17 ± 7 min, a reasonable time period for procedures such as peritoneal closure and only a short period (9 ± 4 min) of profound blockade (twitch height depressed >95%) during which antagonism of the blockade may be difficult. With preexisting metocurine blockade, however, this maintenance dose of vecuronium led to an almost fivefold increase in the duration of surgical relaxation. More importantly, with prolonged 5% recovery time, this blockade may not be readily reversible.[5,6] The magnitude of the difference between groups was only studied at one vecuronium maintenance dose. The degree of synergism may be different at other doses. Hence, it is possible that a smaller dose of vecuronium in the metocurine group could provide sufficient relaxation of a more appropriate duration. Clearly, however, this study demonstrates that the use of vecuronium 0.015 mg/kg after preestablished metocurine-induced neuromuscular blockade does not result in a short duration of action.

TABLE 1. Magnitude and Duration of Response to Vecuronium 0.015 mg/kg Following 25% Recovery from Metocurine 0.3 mg/kg or Vecuronium 0.1 mg/kg

	Vecuronium	Metocurine	*P*
Age (yr)	3 ± 17	41 ± 16	0.69 (NS)
Weight (kg)	70 ± 12	73 ± 13	0.51 (NS)
Maximum response (%)	94 ± 6	100	0.003
5% recovery (min)	9 ± 4	49 ± 9	0.0001
25% recovery (min)	17 ± 7	79 ± 14	0.001

Values are given as mean ± SD; n = 12 in each group.

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